

### **REMARKS**

Upon entry of the present amendment, claims 1-18 and 33-53 will be pending in this application. Claims 1, 8, 33, and 43 have been amended and new claims 50-53 added. Support for the amendments appears in claim 1 and in the amended claims themselves. No new matter is added.

Applicants note that a Supplemental Information Disclosure Statement was submitted for this case on December 11, 2003, and respectfully request return of an initialed Form 1449 in the next substantive communication from the Examiner.

#### **Double Patenting Rejections**

Claims 5, 8-10, 12-18, 43-44 and 46-49 are provisionally rejected under 35 U.S.C. §101 as claiming the same invention as claims 1, 20-22, 25-27, 29, 31-33, 58-59, 61, 63, 65 and 66 of copending Application No. 10/256,023 (‘the ‘023 application’). The rejection is traversed to the extent it is applied to the claims as amended.

Claims 1, 8 and 43, from which the remaining claims subject to the rejection depend, have been amended to specify, *inter alia*, that the claims require a water-soluble inclusion complex consisting essentially of nano-sized water-insoluble lipophilic particles and an amphiphilic polymer. This feature of the claims is not present in the cited claims of the ‘023 application. Thus, the claims as amended are not drawn to the same invention as the cited claims of the ‘023 application. Reconsideration and withdrawal of the rejection for statutory double-patenting is requested.

#### **Rejection under 35 U.S.C §102(e)**

Claims 1-7 are rejected as anticipated by Parikh et al., U.S. Pat. No. 6,228,399 (“Parikh”). The rejection is traversed to the extent it is applied to the claims as amended.

Claim 1, from which depends claims 2-7, has been amended to require that the hydrophilic inclusion complex consists essentially of nano-sized water-insoluble lipophilic particles and an amphiphilic polymer. Parikh does not describe a hydrophilic inclusion complex that includes essentially only these features. Instead, it describes a microparticle that includes a drug, a surfactant that is typically a phospholipid, and a least one surface modifier (See Abstract); the surface modifier can be a polymer such as methylcellulose and hydroxycellulose (see, e.g. col. 3, lines 20-28). The

complex of claim 1 therefore does not encompass the microparticles of Parikh because the transitional phrase “consisting essentially of “ in the claim excludes agents such as phospholipids from the claimed hydrophilic inclusion complex. Applicants request reconsideration and withdrawal of the rejection for anticipation.

**Rejection under 35 U.S.C §103(a)**

Claims 8-18 and 33-49 are rejected as obvious over the combination of Rolfes et al., U.S. Pat. No. 6,221,399 (“Rolfes”), in view of Parikh. The rejection is traversed to the extent it is applied to the claims as amended.

It is well recognized under U.S. law, that any rejection of a claim for obviousness over a combination of prior art references must establish that: (1) the combination produces the claimed invention; and (2) the prior art contains a suggestion or motivation to combine the prior art references in such a way as to achieve the claimed invention.<sup>1</sup> The motivation to modify the prior art must flow from some teaching in the art that suggests the desirability or incentive to make the modification needed to arrive at the claimed invention.<sup>2</sup> The mere fact that the prior art could be modified does not make the modification obvious unless the prior art suggests the desirability of the modification.<sup>3</sup>

Claims 8, 33, and 43, from which the remaining claims subject to the rejection depend, have been amended to require that the amphiphilic polymer molecule in the aqueous solvent is a single amphiphilic polymer. The claims have also been amended to require that the water soluble inclusion complex formed in the recited methods consists essentially of nano-sized water-insoluble lipophilic particles and an amphiphilic polymer.

Methods with these features are not taught or suggested by the combination of Rolfes and Parikh. Rolfes describes a solid interpolymer matrix comprising complexes of two or more complementary polymers (*See*, Rolfes at column 7, lines 1-23). The reference further reports that the two complementary polymers, which are capable of complexing with each other, produce a precipitate or gel (*i.e.*, a physical 3-dimensional network is formed). Rolfes also describes a method using complementary polymers or polymers which form interpolymer matrixes by complexing with

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<sup>1</sup> *In re Vaeck*, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991).

<sup>2</sup> *In re Napier*, 34 U.S.P.Q.2d 1782, 1784 (Fed. Cir. 1995).

<sup>3</sup> *In re Laskowski*, 10 U.S.P.Q.2d 1397, 1399 (Fed. Cir. 1989).

each other. However, Rolfes does not teach, and lacks any suggestion of, a method for making inclusion complexes with a single amphiphilic polymer, as the amended claims expressly require.

Furthermore, Rolfes describes the active agent as becoming incorporated into the interpolymer complex, *e.g.*, embedded or encapsulated in the interpolymer complex (*See*, Rolfes at column 7, lines 26-28 and lines 32-33). Specifically, the incorporation of the active agent into the interpolymer complex creates a viscous environment that encourages a homogeneous distribution of the dispersed drug within the polymer matrix. Rolfes does not teach direct complex formation between the polymer and the active agent, which results from Applicants' claimed methods.

Parikh does not cure the deficiencies of Rolfes. As discussed above, Parikh does not describe a hydrophilic inclusion complex now required by the claims, *i.e.*, a hydrophilic inclusion complex that consists essentially of nano-sized water-insoluble lipophilic particles and an amphiphilic polymer, or a method of making the hydrophilic inclusion complex.

Parikh also fails to teach or suggest non-interpolymer complexes or inclusion complexes comprising a single amphiphilic polymer, as claimed here. Further, Parikh teaches the addition of surfactants as a key component of the production of microparticles, whereas the nano-particles of the present invention do not include surfactants (*See*, Parikh at column 1, line 60 - column 2, line 30).

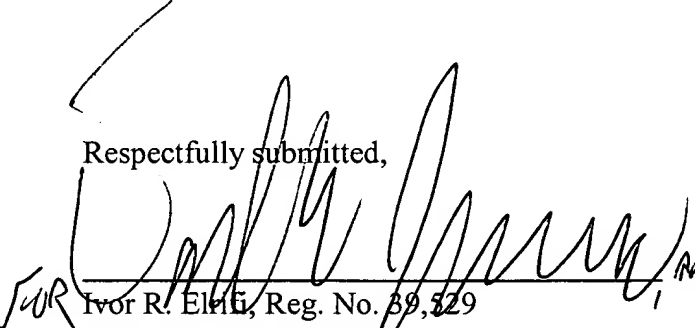
In summary, Applicants submit that the combination of Rolfes and Parikh does not teach or suggest the claimed invention and that one of ordinary skill in the art combining the teachings of Rolfes and Parikh would not produce the present invention. In view of the above, withdrawal of the present rejection is respectfully requested.

In view of the aforementioned remarks and amendments, the Applicants believe that each of pending claims is in condition for allowance. Reconsideration, withdrawal of the rejections, and passage of the case to issue is respectfully requested. A notice to this effect is earnestly solicited.

If, upon receipt and review of this amendment, the Examiner believes that the present application is not in condition for allowance and that changes can be suggested which would place the claims in allowable form, the Examiner is respectfully requested to call Applicant's undersigned counsel at the number provided below.

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Respectfully submitted,

  
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